

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re PATENT APPLICATION of

PEPYS

Application No.: 09/737,544

Filed: December 18, 2000

Title: TREATMENT AND PREVENTION OF TISSUE DAMAGE

Group Art Unit: 1617

Confirmation No.: 1521

Examiner: Shengjun WANG

KATZ DECLARATION BY PROFESSOR MARK B. PEPYS

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Mark B. Pepys, hereby declare as follows:

- (1) I am Professor of Medicine and Head, Department of Medicine, Hampstead Campus, Royal Free and University College Medical School, London, U.K., and have worked in the field of chemical, biological, and clinical investigation of C-reactive protein (CRP) for 30 years.
- (2) I am the sole inventor of U.S. Patent Application No. 09/737,544, entitled "Treatment and Prevention of Tissue Damage" ("the '544 application").
- (3) I have invented a method for selecting a pharmaceutical for treating or preventing CRP-mediated tissue damage in a subject comprising identifying and selecting a compound that inhibits the binding of CRP to an autologous or extrinsic ligand thereof, and a method for treating or preventing C-reactive protein (CRP)-mediated tissue damage comprising administering to a subject in need thereof an effective amount of a compound capable of inhibiting the binding of CRP to an autologous or extrinsic ligand thereof. Original claims 1-25 and 39-48 of the '544 application that were elected for examination are directed to embodiments of my invention pertaining to a method for treating or preventing CRP-mediated tissue

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Attorney Docket No. 068800-0275486

damage a subject in need thereof comprising administering to the subject an effective amount of phosphocholine or a derivative thereof that inhibits the binding of CRP to an autologous or extrinsic ligand thereof.

(4) I have read and am familiar with the official action issued by the U.S. Patent and Trademark Office and dated September 2, 2005, in connection with the '544 application.

(5) I make this declaration in response to the official action issued 2005, in which claims 1-25 and 42-56 were rejected under 35 U.S.C. § the claimed invention allegedly would have been obvious to a person o in the art at the time the invention was made, in view of Bhakdi et al. Thromb. Vasc. Biol., 1999, 19:2348-2354), in view of Griselli et al. (December 20, 1999, 190(12): 1733-1739), further in view of Yedgar et al. (U.S. Patent No. 5,064,817) and Wissner et al. (U.S. Patent No. 4,640,913).

(6) I have reviewed the above-identified references cited by the examiner, i.e., Bhakdi et al. (1999), Griselli et al. (1999), Yedgar et al. (U.S. Patent No. 5,064,817) and Wissner et al. (U.S. Patent No. 4,640,913).

(7) The Griselli et al. publication, of which I am a co-author, relates to the invention that is disclosed in the '544 application, and describes experimental results that are disclosed in the '544 application. For example, Figures 1 and 2 and Tables 1 and 2 of the Griselli et al. reference are identical to Figures 1 and 2 and Tables 2 and 3 of the '544 application.

(8) Pursuant to 37 C.F.R. §1.132, I hereby declare that I am the sole inventor of the subject matter disclosed in the Griselli et al. publication. The other authors of the publication, Massimo Griselli, Jeffrey Herbert, Winston L. Hutchinson, Kenneth M. Taylor, Muhammed Sohail, and Thomas Krausz, worked under my direction and supervision and were not co-inventors. See In re Katz, 215 U.S.P.Q. 14 (CCPA 1982).

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At the time the work reported in the Griselli et al. article was performed, Massimo Griselli was an M.S. (Surgery) student, and I was his supervisor; Jeffrey Herbert was a clinical scientist (a member of staff in the department); Winston Hutchinson was a Principle Research Fellow (also member of staff in the dept); Professor Kenneth Taylor was joint supervisor of Massimo Griselli (Dept. of Surgery); and Muhammed Sohail and Thomas Krausz (both of whom are histopathologists) were acting as collaborators.

The work reported in the Griselli et al. reference was entirely my idea, including the experimental approach, all aspects of the experiments and the writing of the manuscript. I organized a suitable team including members of his own laboratory and others with the necessary expertise. Thus I enlisted the collaboration of K. Taylor, the Professor of Cardiac Surgery, who provided M. Griselli, a trainee surgeon, to do the rat surgery, and T. Krausz, the Professor of Histopathology, who provided M. Sohail, a trainee histopathologist, to do the histology. The other authors thus made essentially technical contributions, albeit at a high level, rather than intellectual contributions to the work.

(9) I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and may jeopardize the validity of the application or any patent issued thereon.

MARK B. PEPYS

Date

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DECLARATION BY PROFESSOR MARK B. PEPYS
PURSUANT TO 37 C.F.R. §1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Mark B. Pepys, hereby declare as follows:

- (1) I am Professor of Medicine and Head, Department of Medicine, Hampstead Campus, Royal Free and University College Medical School, London, U.K., and have worked in the field of chemical, biological, and clinical investigation of C-reactive protein (CRP) for 30 years.
- (2) I am the sole inventor of U.S. Patent Application No. 09/737,544, entitled "Treatment and Prevention of Tissue Damage" ("the '544 application").
- (3) I have invented a method for selecting a pharmaceutical for treating or preventing CRP-mediated tissue damage in a subject comprising identifying and selecting a compound that inhibits the binding of CRP to an autologous or extrinsic ligand thereof, and a method for treating or preventing C-reactive protein (CRP)-mediated tissue damage comprising administering to a subject in need thereof an effective amount of a compound capable of inhibiting the binding of CRP to an autologous or extrinsic ligand thereof. Original claims 1-25 and 39-48 of the '544 application that were elected for examination are directed to embodiments of my

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invention pertaining to a method for treating or preventing CRP-mediated tissue damage in a subject in need thereof comprising administering to the subject an effective amount of phosphocholine or a derivative thereof that inhibits the binding of CRP to an autologous or extrinsic ligand thereof. Prior to my present invention, it was not known that CRP is capable of mediating tissue damage, or that a compound that inhibits the binding of CRP to an autologous or extrinsic ligand thereof such as phosphocholine or a derivative thereof could be administered to a subject to successfully treat or prevent CRP-mediated tissue damage.

(4) I have read and am familiar with the official action issued by the U.S. Patent and Trademark Office dated September 2, 2005, in connection with the '544 application.

(5) I make this declaration in response to the official action issued September 2, 2005, in which claims 1-25 and 42-56 were rejected under 35 U.S.C. §103(a), because the claimed invention allegedly would have been obvious to a person of ordinary skill in the art at the time the invention was made, in view of Yeh et al. (U.S. Patent No. 6,764,826), in view of Bhakdi et al. (Arterioscler. Thromb. Vasc. Biol., 1999, 19:2348-2354), and further in view of Yedgar et al. (U.S. Patent No. 5,064,817) and Wissner et al. (U.S. Patent No. 4,640,913).

(6) I have reviewed the above-identified references cited by the examiner, i.e., Yeh et al. (U.S. Patent No. 6,764,826), Bhakdi et al. (1999), Yedgar et al. (U.S. Patent No. 5,064,817) and Wissner et al. (U.S. Patent No. 4,640,913).

(7) The effective date of U.S. Patent No. 6,764,826 of Yeh et al., which is cited as the primary reference in the rejection of claims 1-25 and 42-56 under 35 U.S.C. §103(a), is June 8, 2000, which is the date that the patent is effective as a 102(e) reference (*see* 37 C.F.R. §1.131(a)(1)). The effective date of U.S. Patent No. 6,764,826 of Yeh et al. is therefore less than a year prior to the filing date of the present application, which was filed on December 18, 2000.

(8) The six claims of U.S. Patent No. 6,764,826 of Yeh et al. are all directed to an in vitro method for screening for modulators of human C-reactive protein. The claims of U.S. Patent No. 6,764,826 of Yeh et al. are therefore directed to subject matter that is different from the subject matter of the rejected claims, which are directed to a therapeutic method for treating or preventing CRP-mediated tissue damage in a subject.

(9) I hereby declare that I invented the subject matter of the rejected claims prior to the effective date of U.S. Patent No. 6,764,826 of Yeh et al., which is June 8, 2000. Evidence of my prior invention is found in Griselli et al., a scientific article published in the Journal of Experimental Medicine (vol. 190 (sec. 12), pages 1733-1739) with a publication date of December 20, 1999. As I declared in a declaration under 37 C.F.R. §1.132 submitted herewith, I am the sole inventor of the subject matter disclosed Griselli et al., as the other authors of the publication worked under my direction and supervision and were not co-inventors. Griselli et al. provides the first publicly disclosed demonstration that CRP is capable of mediating tissue damage in a mammal. The materials and methods, experimental results shown in Figures 1-2 and Tables I-II, and the discussion of the significance of these results with respect to clinical benefits provided by to patients treating or preventing CRP-mediated tissue damage associated with traumatic, infectious, inflammatory, and neoplastic tissue-damaging conditions, described on pages 1734-1737 of Griselli et al., are identical to materials and methods, experimental results, and discussion, found on pages 25-34, 36, and 37 of the application filed on December 18, 2000. After the publication of Griselli et al. on December 20, 1999, the inventor has worked diligently on the claimed invention, as evidenced by the filing of the present application, the publication of Gill et al. in 2004 (Journal of Cerebral Blood Flow and Metabolism, 24(11:1214-1218)), which describes experimental results demonstrating that CRP mediates tissue damage associated with cerebral infarct, and the award to the inventor in 2004 by the U.S. National Institutes of Health of a research grant of \$861,200 over 4 years entitled "*Targeting C-reactive protein in atherothrombotic disease.*"

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(10) I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and may jeopardize the validity of the application or any patent issued thereon.

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